



UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/250,466	02/16/1999	ILSE CHUDоба	RPE-27	2088

7590 08/14/2003

JOHN B HARDAWAY III
HARDAWAY LAW FIRM
P O BOX 10107
FEDERAL STATION
GREENVILLE, SC 296030107

EXAMINER

MORAN, MARJORIE A

ART UNIT	PAPER NUMBER
----------	--------------

1631

DATE MAILED: 08/14/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/250,466

Applicant(s)

CHUDOBA ET AL.

Examiner

Marjorie A. Moran

Art Unit

1631

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 04 October 2001.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 31-55 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 31-55 is/are rejected.
- 7) ☒ Claim(s) 50,52 and 53 is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____
- 4) ☐ Interview Summary (PTO-413) Paper No(s). _____
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: _____

Continued Prosecution Application

The request filed on 10/4/01 for a Continued Prosecution Application (CPA) under 37 CFR 1.53(d) based on parent Application No. 09/250,466 is acceptable and a CPA has been established. The preliminary amendment filed with the CPA has been entered and an action on the CPA follows. Claims 31-55 are pending.

All rejections and objections not reiterated below are hereby withdrawn. It is noted that the Remarks section of the response filed 10/4/01 indicates that an interview was scheduled for 10/17/01; however, there is no indication in the pending file that this interview did in fact occur. The examiner for this application has changed. If an interview did take place with the previous examiner, applicant is kindly requested to file an Interview Summary indicating the substance of the interview so that the pending record will be complete. If the interview did not take place, and applicants still wish to have an interview with the current examiner after review of the following office action, applicant is encouraged to contact the examiner at the number set forth below. The examiner regrets any inconvenience to applicant.

Claim Objections

Claims 50, 52 and 53 are objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. Claim 51 depends from claim 50, and limits a step of aligning. Claim 51 depends from claim 47; neither claim 47 nor claim 51 recites an alignment step, therefore claim 50 fails to limit the subject matter of a parent claim, and is improperly dependant. Claim 53 depends from itself and therefore recites improper

Art Unit: 1631

dependency. Claim 52 depends from claim 53 (which is improperly dependant), and is therefore also improperly dependant.

Claim Rejections - 35 USC § 112, 1st paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 50, 52-53, and 55 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a NEW MATTER rejection

An automatic step of alignment, as recited in claim 50, is new matter. Original claim 22 limited "positional correction of... bondings" to take place automatically; however the positional corrections of original claim 22 do not appear to be the same as the alignment of images with respect to bondings, as recited in the instant claims. AS the alignment of claim 49 is the only alignment recited in the pending claims, it is assumed that this is the alignment which is limited to be automatic in claim 50. Page 7 of the originally filed specification discloses "automatic correction" by correlating images with a labeled (calibration) probe. Again, a "correction" does not appear to be the same as an alignment between images and bondings, as recited in the claims. Applicant does not point to support in the originally filed specification or claims for the limitation of new claim 50, and none is apparent, as set forth above, therefore claim 50 is rejected as reciting new matter.

Claim 53 recites "fluorescence-labeled DNA particles", which is new matter. Original claim 24 recited "fluorescence-labelled DNA probes" and original claim 25 recited "fluorescence-labelled particles", but the original claims did not recite "fluorescence-labeled DNA particles" anywhere. The specification sets forth definitions of "labeled detector molecules" on pages 3-4, but the term "fluorescence-labeled DNA particles" is not found anywhere in the specification. Applicant does not point to support in the originally filed specification or claims for the limitation of new claim 53, and none is apparent, as set forth above, therefore claim 53 is rejected as reciting new matter.

Specific steps of separately providing a first and second set of labeled detector molecules, as recited in claim 55, in new matter. Original claim 1 recited a single step of providing different sets of detector molecules. Original claim 4 limited the *bonding reaction* of claim 1 to be carried out sequentially or simultaneously; however, the bonding reactions of claim 1 clearly occur in step (b), AFTER the step of providing detector molecules, therefore original claim 1 does not provide support for the separate providing steps of new claim 55. The specification, on pages 9-10, exemplifies a method wherein probes are generated and labeled. The specification does not disclose whether the probes were labeled separately, or in a mixture, nor whether the labeled probes are separated before use in the method. The originally filed specification does not teach distinct, separate steps of providing different sets of labeled probes in the inventive method anywhere. Applicant does not point to support in the originally filed specification or claims for the limitations of new claim 55, and none is apparent, as set forth above, therefore claim 55 is rejected as reciting new matter.

Claim Rejections - 35 USC § 112, 2nd paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 47-54 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 47 recites the term "said probes" in line 4. It is unclear if the antecedent basis for this term is intended to be the "calibrating probes" of line 2 or different probes, therefore claim 47 is indefinite.

Claim 48 recites a step of correcting positional transformations of bondings "by comparison of calibrating probes". It is unclear what the comparison is intended to be between; i.e. calibrating probes to other calibrating probes, or calibrating probes to bondings, or calibrating probes to the detector molecules of line 2, therefore the claim is indefinite.

Claim 50 recites the limitation "said step of aligning" in line 1. There is insufficient antecedent basis for this limitation in the claim, therefore claim 50 is indefinite. Claim 50 depends from claim 51, which does not recite an alignment step. This rejection and the objection set forth above with regard to claim 50 may be overcome by amending claim 50 to depend from claim 49, if such is consistent with applicant's intent.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

Art Unit: 1631

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 31-44 and 55 are rejected under 35 U.S.C. 102(e) as being anticipated by GARINI et al. (US 5,817,462, filed 4/22/1996).

GARINI teaches a method of for identifying differences in chromosomes (biopolymers) wherein various sets of fluorescently labeled probes are provided, such that at least some of the sets of probes hybridize or "bond" to the same region (band) of a chromosome, the probes are exposed to chromosomes. And the hybridization intensity and presence are evaluated such that differences can be identified (col's 48-52, Examples 5-8, col. 25, lines 53-59, and col. 26, lines 39-44), thereby anticipating claims 31, 35, 37-39, and 41. GARINI teaches that is fluorescently labeled probes may be DNA, teaches that his different sets of probes may be labeled with different fluorophores (see Example 8), scanning along a longitudinal axis (col. 51, lines 55-60), and teaches simultaneous hybridization (col. 50, lines 2-11), thereby anticipating claims 34, 40, and 42-44. GARINI teaches that his method can be used on *in situ* samples as well as on fixed, immobilized samples (col. 26, lines 15-18 and col. 32, lines 10-14), thereby anticipating claims 32-33 and 36. GARINI also teaches that his probes may be provided individually and regrouped (Example 9 and col. 28, lines 50-54), thereby anticipating claim 55.

Claims 31-43 and 55 are rejected under 35 U.S.C. 102(e) as being anticipated by MIRZABEKOV et al. (US 6,458,584, filed Dec. 23, 1996).

Art Unit: 1631

MIRZABEKOV teaches a method of identifying differences between biopolymers (genes) by hybridization of differently labeled DNA or RNA probes which recognize the same area of a gene, then detecting the presence and intensity of the probes and detecting the difference (col. 7, lines 31-36, col. 8, lines 45-65, and col. 14, lines 34-55), thereby anticipating claims 31, 34-35, 37-40, and 42-43. MIRZABEKOV teaches that sample may be immobilized on a microchip (col. 12, Example 2), and teaches both simultaneous and sequential hybridization to his probes (col. 8, lines 36-55), thereby anticipating claims 32-34 and 55. MIRZABEKOV further teaches in situ hybridization (col. 16, lines 30-36), thereby anticipating claim 36. In addition, MIRZABEKOV teaches use of a dye-labeled probe as a standard; i.e. a calibrating probe (col. 18, lines 44-48).

Claims 31-35 and 55 are rejected under 35 U.S.C. 102(b) as being anticipated by SHALON et al. (Genome Research (1996), volume 6 (7), pp. 639-645).

SHALON teaches a method of identifying differences between yeast chromosomes wherein probes which "bond" to the same "area" or element of a chromosome are labeled with two different fluorophores, allowed to hybridize on an array, and the hybridization signals detected and used to identify differences between the chromosomes (pp. 641-642). SHALON teaches that detection in his method includes measuring hybridization intensity (p. 644: detection and Analysis), thus claims 31-35 and 37-43 are anticipated. SHALON teaches that his probes are supplied separately before application to his matrix (p. 644), therefore claim 55 is anticipated.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 31-46 are rejected under 35 U.S.C. 103(a) as being unpatentable over GARINIE et al. (US 5,817,462) in view of CABIB et al. (US 5,784,162).

Claim 31 is directed to a method of identifying differences between biopolymers by providing two or more sets of detector molecules which specifically bind to a region of the biopolymers, wherein the sets of detector molecules are differently labeled, exposing biopolymers to the labeled detector molecules, and detecting the presence and intensity of bonding between the polymers and detector molecules in order to identify differences between the biopolymers. Claim 55 is directed to a similar method wherein two sets of detector molecules are provided separately. Claims 32-33 limit the biopolymers to be immobilized, specifically on a carrier or in a matrix. Claim 33 limits the bonding between a polymer and each of the detector molecules to be simultaneous or successive. Claims 35-36 limit the bonding to

Art Unit: 1631

be hybridization or an antibody/antigen reaction, specifically in situ hybridization. Claims 37-41 limit the biopolymers to be nucleic acids or peptides, specifically DNA or RNA, more specifically chromosomal DNA. Claims 42-43 limit the detector molecules to be nucleic acids or antibodies, specifically nucleic acids selected from chromosome region-specific DAN libraries, limits the labels of one set to be different from those of another set, and limits the labels to fluorescent dyes. Claim 44 limits the method to further comprise longitudinal scanning and recording of intensities of the labels. Claim 45 limits the method to further comprise providing at least one localized calibrating probe comprising calibrating labels. Claim 46 limits the calibrating labels to comprise all of those on the detector molecules.

GARINI teaches a method of identifying differences in chromosomes (biopolymers) using various sets of fluorescently labeled probes, as set forth above. GARINI specifically teaches that the intensity at each labeled site can be measured in order to calculate the amount of DNA (biopolymer) present in a sample; e.g. to a chromosomal site, and teaches that multiple fluorescent probes can be quantified (col. 26, lines 38-43). GARINI does not teach use of calibrating probes comprising calibrating labels.

CABIB teaches that standard calibrating dyes can be used in methods similar to that taught by GARINI in order to determine absolute concentrations of biopolymer in a sample (col. 29, lines 13-21).

It would have been obvious to one of ordinary skill in the art at the time of invention to have provided probes with calibrating dyes (labels), as taught by CABIB, in the method of GARINI where the motivation would have been to quantify the amounts of specific genes/chromosomal DNA present in each sample to which the probes are bound, as taught by both GARINI and CABIB.

Art Unit: 1631

Conclusion

Claims 31-55 are rejected.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Marjorie A. Moran whose telephone number is (703) 305-2363. The examiner can normally be reached on Monday to Friday, 7:30 am to 4 pm EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Woodward can be reached on (703) 308-4028. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 308-4242 for regular communications and (703) 872-9306 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 305-3524.

mam
August 8, 2003

MARJORIE MORAN
PATENT EXAMINER

